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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/790,043	01/28/97	PAYNE D	GM50005

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EXAMINER	
PRIEBE,S	

ART UNIT	PAPER NUMBER
1819	5

DATE MAILED: 12/23/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/790,043	Applicant(s) Payne et al.
	Examiner Scott D. Priebe, Ph.D.	Group Art Unit 1819

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-24 is/are pending in the application.

Of the above, claim(s) 12-24 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-11 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

In the original claim set, claim numbers 14 and 15 were skipped. Consequently, claims originally numbered as claims 16-26 were re-numbered as claims 14-24, and applicant should correct their copy of the claims accordingly

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-11, drawn to nucleic acids and a method of making a polypeptide and a method of making a cell using the nucleic acids, classified in class 536, subclass 23.7; class 435, subclass 69.1; and class 435, subclass 172.3.

II. Claims 12 and 13, drawn to a polypeptide, classified in class 530, subclass 350.

III. Claim 14, drawn to an antibody, classified in class 530, subclass 388.4.

IV. Claim 15, drawn to an antagonist or inhibitor of an enzyme, class and subclass dependent on species.

V. Claim 16, drawn to a method of treatment with a polypeptide, classified in class 424, subclass 94.4.

VI. Claim 17, drawn to method of gene therapy, classified in class 514, subclass 44.

VII. Claim 18, drawn to method of treatment with an enzyme antagonist/inhibitor, classified in class 514, subclass dependent upon species of compound.

VIII. Claim 19, drawn to a diagnostic method comprising sequencing a nucleic acid, classified in class 435, subclass 6.

IX. Claim 20, drawn to a diagnostic method comprising detecting a protein, classified in class 435, subclass 4.

X. Claim 21, drawn to a cell-based assay for an inhibitor of a polypeptide, classified in class 435, subclass 29.

XI. Claims 22 and 24, drawn to a method of vaccination using a polypeptide, classified in class 514, subclass 2+.

XII. Claims 23 and 24, drawn to a method of immunization using nucleic acid expressing a protein, classified in class 514, subclass 44.

Claim 24 recites a misjoined Markush group in that the recited nucleic acid and protein do not share a common structural feature , a common function, or a common utility. Therefore, claim 24 was placed in invention XI for the embodiment comprising a protein and in invention XII for the embodiment comprising a polynucleotide.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and VI, VIII, and XII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that

product (MPEP § 806.05(h)). In the instant case the nucleic acids of invention I can be used in any of the methods of inventions I, making a polypeptide or a cell; VI, gene therapy; VIII, diagnostic assay; and XII, method of immunization.

Invention II and inventions V, IX and XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptides of invention II can be used in any of the methods of inventions V, treatment with a polypeptide; IX, diagnostic assay for the polypeptide; and XI, vaccination using the polypeptide.

Invention IV and inventions VII and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antagonist or inhibitor of invention III can be used in either the method of treatment of invention VII or the screening method of invention X, in so much as the inhibitor would have been a known compound among others that were screened.

Inventions I, VI, VIII, and XII; inventions II, V, IX and XI; invention III; and inventions IV, VII and X are unrelated. Inventions are unrelated if it can be shown that they are not

disclosed as capable of use together, or they have different modes of operation, or they have different functions, or they have different effects. (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions I-IV are drawn to structurally and functionally different compounds, i.e. nucleic acids, enzyme polypeptides, , antibodies, and antagonists or inhibitors of the polypeptide. Each of these distinct compounds have different functions and effects. Inventions VIII and XII, inventions V, IX and XI; and inventions VII and X are methods which use the structurally and functionally different compounds, and each of the sets of methods have different modes of operation. None of the methods use invention III.

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the polypeptide of invention II could be purified from non-recombinant bacteria which express the polypeptide.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, the complete search required for each invention is not required for each of the other inventions, and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Edward Gimmi on 12/3/97 a provisional election was made with traverse to prosecute the invention of group I, claims 1-11. Affirmation of this election must be made by applicant in responding to this Office action. Claims 12-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Drawings

The drawings are objected to by the Examiner because "Fig. 2" should be --Figure 2A-- and "Fig. 2A" should be --Figure 2B-- if the sequence is to be shown on separate pages. Correction is required.

Specification

The disclosure is objected to because of the following informalities: The specification refers to "Figure 2" but not "Fig. 2A". Throughout the specification, SEQ ID NO: 2 is used to refer to the amino acid sequence of FAB I and SEQ ID NO: 1 to the nucleotide sequence. However, SEQ ID NO: 1 is an amino acid sequence and SEQ ID NO: 2 is a nucleotide sequence.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1-3 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding amino acids 1-256 of SEQ ID NO: 1, does not reasonably provide enablement for polynucleotide sequences having less than 100% identity with the region of such a polynucleotide that encodes amino acids 1-256 of SEQ ID NO: 1, or a part of this coding region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-3 and 7-11 are broadly drawn to, or recite as a critical limitation, a polynucleotide that has at least 70% sequence identity to a polynucleotide that encodes amino acids 1-256 of SEQ ID NO: 1. First, claim 1 is indefinite as it is not clear which part of the reference polynucleotide encoding the amino acid sequence the claimed polynucleotide must have 70% identity with. Since such a reference polynucleotide, e.g. a cloning vector comprising sequences consisting of the recited coding sequence, may encode the recited amino acid sequence while also comprising other unspecified polynucleotide sequences, the claimed polynucleotide need have no sequences corresponding to the region of the reference polynucleotide encoding the amino acid sequence, e.g. a cloning vector backbone. Therefore the open language of the claim can be interpreted to include any and all unspecified nucleotide sequences. In addition for claim 7, the recited deposited clone does not comprise a cDNA sequence according to the specification, but rather is the genomic source of the polynucleotide whose sequence is set forth as SEQ ID NO: 2 (see para. bridging pages 14-15). Consequently, the mature polypeptide recited in claim 7 could be interpreted to refer to any staphylococcal protein, not just the polypeptide whose sequence is set forth as SEQ ID NO: 1. The specification does not describe how to make and use any and all such unspecified sequences which the claims appear to embrace.

Rather, the specification describes how to make and use polynucleotides encoding the *S. aureus* FAB I protein, whose sequence is set forth in SEQ ID NO: 1, and the genomic sequence encoding it isolated from strain WCUH29, set forth as SEQ ID NO: 2, and suggests that polynucleotides with as little as 70% sequence identity to a polynucleotide encoding the recited

amino acid sequence can also be used. It is noted that over the coding region, the reference polynucleotides can have as little as 66% sequence identity with each other due to the degeneracy of codon sequences. Therefore a polynucleotide with as little as 70% sequence identity over a region corresponding to the coding region of the reference polynucleotide, can have as little as 46% (70% of 66%) nucleotide sequence identity with a natural *S. aureus* sequence encoding FAB I, such as that set forth as SEQ ID NO: 2. It is also noted that such a polynucleotide might encode a polypeptide with as little as 70% sequence identity to SEQ ID NO: 1, if the nucleotide differences lead to codons specific for different amino acids or introduce a stop codon. The specification teaches how to use the claimed polynucleotides to make FAB I polypeptides of fragments thereof for making antibodies and for screening assays for compounds that enhance or inhibit the function of FAB I or express a fragment or all of FAB I for therapeutic treatments, e.g. immunization, or to use as hybridization probes for sequences which have at least 95% sequence identity with the probe sequence, presumably natural sequences which encode FAB I or as PCR primers to amplify a natural sequence, such as might be used for a diagnostic assay for the presence of *S. aureus*.

Regardless of the use of the polynucleotides, the uses taught in the specification require that either the nucleotide sequence or amino acid sequence be nearly identical to a natural nucleotide or amino acid sequence of an FAB I protein, mostly the *S. aureus* FAB I given that the claims are limited to the *S. aureus* FAB I sequence as the amino acid sequence encoded by the reference nucleic acid. Where the use requires polynucleotides encoding an active FAB I protein,

it is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see Ngo, pp. 433 and 492-495). The specification contains no guidance or citations of relevant prior art that would inform the skilled artisan of which amino acid residues of SEQ ID NO: 1 could be altered without adversely affecting its folding or its biological activity. For polynucleotides encoding a FAB I polypeptide or fragment thereof for inducing an immunological response, such as for the production of antibodies or for immunization, the specification does not teach which fragments of the natural FAB I protein might be sufficiently antigenic or immunogenic for such purposes, but more to the point, how such peptides could be altered by substituting, inserting or deleting amino acids to retain or improve the antigenic or immunogenic properties of the peptide. This latter point is key for claims 9-11 read on *inter alia* cells *in vivo,* method of making cells *in vivo* and method for making a polypeptide from such cells *in vivo* for genetic immunization as taught in the specification. With respect to polynucleotides to serve as probes or primers, the corresponding nucleic acids of *Anabaena, Escherichia, Salmonella, Hemophilus* and *Mycobacterium* bacteria and *Brassica*, a plant, share no more than 56% sequence similarity over the region of nucleotides 440-756, and as taught in the specification (page 3), the overall amino acid sequence identity with the *Escherichia, Salmonella, Mycobacterium* and *Brassica* FAB I proteins share less than 35% sequence identity with the *S. aureus* FAB I. Thus the claimed nucleic acids would not appear to be suitable as

hybridization probes for related sequences from Gram negative bacteria, cyanobacteria, or plants. The specification teaches no other class of organisms other than *S. aureus* for which one skilled in the art might expect the claimed polynucleotides to be useful as a probe or primer for FAB I nucleic acids. Neither the specification nor the prior art provides sufficient information to the skilled artisan to determine which among the claimed polynucleotides would be useful for any one of the disclosed uses, i.e. which sequence alterations in SEQ ID NO: 1 would at least preserve the properties of encoding functional FAB I, encoding antigenic or immunogenic peptides that would bind to a natural FAB I, or alterations of SEQ ID NO: 2 which hybridize effectively with a natural nucleic acid encoding an FAB I protein. To determine which of the high number of sequences encompassed by the claims could be used for the disclosed purposes would require excessive trial and error experimentation. As set forth in *In re Fisher,* 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic

sequences may not find sufficient support under 35 USC 112, 1st para., if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. This is the case here, where specification discloses only a single amino acid sequence and nucleotide sequence having the necessary properties for the disclosed uses. In light of the limited guidance for making polynucleotides having the necessary properties and the failure of state of the prior art to provide the information missing from the specification, the limited number of working examples, the unpredictable nature of determining the useful sequences *a priori*, the excessive trial and error experimentation that would then be required to identify the useful sequences within the claimed groups of polynucleotides, it would require undue experimentation to make and use the polynucleotides commensurate in scope with the claimed invention for the uses disclosed in the specification.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 are indefinite for recitation of "a 70% identity to a polynucleotide" in claims 1 and 7. As discussed on page 8 line 12 to page 9 line 2, of the specification, there are several different methods for calculating the percent sequence similarity or identity of two polynucleotide sequences. These methods do not all yield the same results in part because of the way in which

insertion/deletion differences are handled, therefore unless one specific method is recited, the metes and bounds of the claim are unclear as they depend solely on the method the skilled artisan would use to determine whether a given polynucleotide fell within the scope of the claimed polynucleotide. Also, with respect to claim 1, it is unclear whether the "70% identity" applies to the entire polynucleotides or just the region of each that corresponds to the region of each that encodes the amino acid sequence recited. It is unclear whether a polynucleotide that has at least 70% identity to that part of the reference polynucleotide that does not include the region encoding the amino acid sequence is to be encompassed by the claim, e.g. would pBR322 be covered by the claim in reference to a polynucleotide comprising pBR322 and a nucleotide sequence encoding the amino acid sequence. The open language of the claim allows this interpretation. With respect to part (c) of claims 1 and 7, it is unclear whether the "15 bases" (--nucleotides-- is preferable over "bases") can be any selected bases in any order, or refers to --15 contiguous nucleotides--.

Claims 1-11 are indefinite for recitation of "SEQ ID NO: 2", which is a nucleotide sequence, not an amino acid sequence.

Claim 4 is indefinite for recitation of "SEQ ID NO: 1", which is an amino acid sequence, not a nucleotide sequence. Also, "nucleotide" should be --nucleotides--

Claim 5 is indefinite for recitation of "comprising nucleotide encoding the amino acid sequence"; "nucleotide" should be replace with --a polynucleotide--.

Claim 6 is indefinite for recitation of "amino acid", which should be --amino acids--.

Claim 7 is indefinite for recitation of "the cDNA contained in NCIMB Deposit No. 40771". As stated in the specification, the DNA set forth as SEQ ID NO: 2 was taken from the genome of *S. aureus* WCUH29 cells, not a cDNA cloned into the strain. Thus, the specification does not disclose a cDNA present in this strain. It is noted that if "cDNA'" is interpreted as genomic DNA, since no cDNA is present in the strain, then claim 7 reads on any *S. aureus* cloned protein coding sequence, or a polynucleotide of at least 70% sequence identity to a *S. aureus* coding sequence.

Claim 10 is indefinite as it is an incomplete method claim reciting no active process steps. The "expressing" of a polypeptide is carried out by the cell, not the one carrying out the method. The claim should recite process steps relating to what one skilled in the art would do to allow the cell to express the polypeptide, e.g. culturing the cells under conditions that lead to expression of the polypeptide.

Claim 11 recites the limitation "the cDNA" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Turnowsky et al. Turnowsky et al. disclose a polynucleotide which encode the *Salmonella typhimurium envM* (FAB I) protein (page 6560). The polynucleotide comprises at least 15 bases of a polynucleotide that encodes SEQ ID NO: 1. The peptide RVNAISAGPIRTL, amino acids 184-196 is present in both the *Salmonella* and *Staph aureus.* FAB I proteins. Therefore the *Salmonella envM* gene is a polynucleotide that comprises a 39 nucleotide sequence, which is at least 15 bases of a polynucleotide that encodes SEQ ID NO: 1. In so much as the FAB I protein sequence disclosed as SEQ ID NO: 1 is that encoded by the genome of the recited deposited clone, the *Salmonella envM* gene is a polynucleotide that comprises a 39 nucleotide sequence, which is an at least 15 bases of a polynucleotide that encodes the same mature polypeptide as NCIMB Deposit No. 40771. Turnowsky et al. also disclose vectors comprising the polynucleotide, methods of making a cell comprising the vector by transforming host cells with the vector, cells comprising the vector, and method of producing the polypeptide encoded thereby by expressing the vector FAB I encoding sequence. (see Abstract and Materials and Methods, pages 6555-6557, col. 1, and page 6561).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claim 9 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim reads on any type of cell including a cell present in an organism, which could be human such as a patient immunized with a polynucleotide expressing a FAB I protein or fragment. Such cells as claimed which are present in a human are non-statutory subject matter since the host cells were originally part of the patient. Amendment of the claim to recite --cultured cell-- would overcome this rejection.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1819 by facsimile transmission. The FAX number is (703) 308-4242 or 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 9 AM to 5 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, Ph.D., can be reached on (703) 308-2035.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SDP

Scott D. Priebe, Ph.D.

Jasemine C. Chambers

JASEMINE C. CHAMBERS, PHD.
SUPERVISORY PATENT EXAMINER
GROUP 1800

December 22, 1997

Examiner